Effects of Cell Stress and Low Density Lipoprotein Concentration on the Localization of Amyloid Precursor Protein

Anna Tarren, Edward Cluett

Amyloid precursor protein (APP) is a single transmembrane protein that is involved with neurite growth, cell adhesion and synaptogenesis. There are two processing routes for APP, one that leads to a normal functioning protein and the other that may lead to an amyloidgenic protein, which is associated with Alzheimer's disease. The processing of APP depends on its location in the cell since it has been found in many compartments of the membrane transport pathway. Current models indicate that "good" processing occurs on the cell surface, and misprocessing occurs in a compartment of the membrane transport system. There is research that shows cholesterol trafficking is also associated with this pathway and evidence strongly suggests that cholesterol plays a role in misprocessing of APP. Previous research in our lab found that cholesterol is transported via membrane tubules. The inhibition of these membrane tubules causes the accumulation of cholesterol, as well as APP, in the endocytic recycling compartment (ERC), marked by Rab11. The ERC is also known as a reservoir for cholesterol. Interestingly, a recent paper has shown that the ERC serves as a central trafficking hub for APP. Dr. Cluett's lab has shown that the distribution of cholesterol affects the processing of APP. Immunofluorescence microscopy experiments were used to double label APP and Rab11 in order to investigate the effects that different concentrations of LDL-derived cholesterol and cellular stress have on the localization and processing of APP. When analyzing the data, it was evident that APP had been dramatically altered under these conditions.